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An Assessment of Health Status among Medical Research Volunteers Who Served in the Project Whitecoat Program at Fort Detrick, Maryland

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Between 1954 and 1973, more than 2,000 men entering military service as conscientious objectors participated in Project Whitecoat as medical research volunteers for the Army's biological warfare defense program. An assessment of self-reported, current health status among 358 "exposed" individuals and 164 unexposed control subjects found no conclusive evidence that receipt of investigational agents was related to adverse health outcomes. No differences in current overall health, current exercise levels, self-reported symptoms, and self-reported medical conditions were seen between the study groups. Possible associations were seen between exposure to antibiotics or other biological agents and self-reported asthma (13.0% vs. 2.4%, relative risk [RR] = 6.00, 95% confidence interval [CI] = 1.03–34.90, $p = 0.050$), as well as between receipt of tularemia vaccine(s) and self-reported asthma (13.3% vs. 2.4%, RR = 6.15, 95% CI = 1.03–36.70, $p = 0.049$) and increased frequency/severity of headaches (35.6% vs. 18.3%, RR = 2.46, 95% CI = 0.99–6.15, $p = 0.074$). However, the size of the population under study was insufficient to assert with confidence that these statistical associations are real.

Introduction

United States government efforts to counter the threat of biological weapons have their genesis in the War Bureau of Consultation, a commission of the National Academy of Sciences that was formed at the request of Secretary of War Harold Stimson in 1941.[1,2] This group recommended the urgent creation of a program of research to address the problem of biological warfare and, in 1942, President Roosevelt authorized Mr. Stimson to establish the War Research Service as a unit of the Federal Security Agency for this purpose. The War Research Service, headed by George Merck (president of Merck Pharmaceuticals), immediately undertook a program of study of biological agents, conducted with "utmost secrecy."[3]

With increasing appreciation of the scope and complexity of a large-scale program of research and development in this area, the War Research Service requested that the U.S. Army Chemical Warfare Service assume responsibility. The initial site selected for the program was Edgewood Arsenal, near Aberdeen, Maryland. In 1943, a small National Guard airfield (Detrick Field) just outside Frederick, Maryland, was purchased by the War Department, and the hub of the operation was moved to the renamed Camp Detrick.

The Office of the Army Surgeon General was involved in the biological warfare research and development program from the time of its inception in 1941, but it was not directly responsible for any activities until 1956, when the U.S. Army Medical Unit at Camp Detrick was activated with a mission to evaluate the threat of biological warfare and to develop appropriate countermeasures.[4] During the same year, Camp Detrick became Fort Detrick. From that time to the present, Fort Detrick has been the home of the nation's biological warfare defense program. The Army Medical Unit was redesignated the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) in 1969. The contributions of USAMRIID and its predecessor to military medical research and national security are legion, and the planned integration of USAMRIID with National Institutes of Health and Department of Homeland Security programs through the formation of a national biodefense campus at Fort Detrick[5] ensures its future leadership role in this area.

Project Whitecoat was the title given to an Army research program "to use human volunteers in medical studies to evaluate the effect of certain biological pathogens upon humans in an effort to determine the vulnerability to attack with biological agents" (W.S. Augerson, 1976, cited in Ref. 4, p 20). The objectives of the studies involved were to develop medical defenses against biological warfare and included techniques for rapid diagnosis, improved therapeutic and prophylactic agents, and development of vaccines against biological weapons and endemic disease threats. The program evolved after a series of meetings in 1954–1955 between representatives of the Army Surgeon General and the Seventh Day Adventist Church. With the background of the Church's philosophy and practice of medical service and encouragement of noncombatancy and its longstanding cooperation with the military in health and medical practice, Project Whitecoat became an accepted and respected vehicle by which conscientious objectors could serve the nation.[4] From its inception in 1954 to its termination in 1973, approximately 2,300 individuals participated in this program, more than 90% of whom were Seventh Day Adventists. The group participated in more than 135 clinical research studies involving exposure to live agents, receipt of investigational vaccines, and studies of metabolic and psychological effects of environmental- and infection-induced stress.[4,6] Most volunteers participated in at least one project, whereas some participated in several. The current study

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14. ABSTRACT

Between 1954 and 1973, more than 2000 men entering military service as conscientious objectors participated in Project Whitecoat as medical research volunteers for the Army's biological warfare defense program. An assessment of self-reported, current health status among 358 "exposed" individuals and 164 unexposed control subjects found no conclusive evidence that receipt of investigational agents was related to adverse health outcomes. No differences in current overall health, current exercise levels, self-reported symptoms, and self-reported medical conditions were seen between the study groups. Possible associations were seen between exposure to antibiotics or other biological agents and self-reported asthma (13.0% vs. 2.4%, relative risk [RR] = 6.00, 95% confidence interval [CI] = 1.03-34.90, p = 0.050), as well as between receipt of tularemia vaccine(s) and self-reported asthma (13.3% vs. 2.4%, RR = 6.15, 95% CI = 1.03-36.70, p = 0.049) and increased frequency/severity of headaches (35.6% vs. 18.3%, RR = 2.46, 95% CI = 0.99-6.15, p = 0.074). However, the size of the population under study was insufficient to assert with confidence that these statistical associations are real.

15. SUBJECT TERMS
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was designed to assess the long-term effects on the health of these men resulting from their involvement in this vital program.

Methods

Study Design

This was a controlled, unblinded, retrospective, cohort study to assess the health status of individuals who volunteered to participate in Project Whitecoat at Fort Detrick, Maryland, during 1955–1973.

Study Population

Approximately 2,300 men who entered military service and were classified as conscientious objectors participated in Project Whitecoat. Most were assigned to Fort Detrick, Maryland, and individuals there were assigned a variety of duties in support of the medical research efforts at the facility. Some worked as technicians in research laboratories, some worked as hospital corpsmen, and others were assigned predominantly administrative duties and responsibilities. Periodically, the group membership was approached regarding interest in participating as volunteers for clinical research studies. Most studies were related to exposure to infectious diseases, for which volunteers would receive proven therapies and occasionally investigational prophylactic agents (e.g., vaccines).

Subjects for this study were recruited from among the membership of the Project Whitecoat alumni group. A total of 358 men who were exposed to an infectious agent or vaccine (study group) and 164 men who participated in research studies as unexposed control subjects (control group) agreed, after signing a written informed consent agreement, to complete a self-administered questionnaire that inquired about health status, ongoing clinical symptoms and signs, reproductive outcomes, and diseases or conditions diagnosed by competent medical authorities. The study was reviewed and approved by the institutional review board at USAMRIID, as well as by the Human Subjects Research Review Board of the U.S. Army Surgeon General.

Exposure Histories

Records for participation in clinical protocols, including receipt of vaccines and disease-causing agents, were obtained by reviewing archives at USAMRIID. The name and type of study in which each volunteer participated were extracted from these records and entered into an automated database for analysis. A total of 197 volunteers received investigational vaccines. The available data did not allow distinction between live vaccines and killed/toxoid products, nor did they allow enumeration of the numbers of different vaccine candidates involved in testing. Two hundred eleven individuals were exposed to disease-causing agents (some of which might have involved exposure to different strains of a given pathogen), and 46 received antibiotics or other therapeutic agents (in physiological or other studies separate from treatment for exposures in other protocols).

Statistical Analyses

The χ^2 and Fisher exact tests were used to compare proportions and the t test was used to compare mean differences between the exposed (study) and control groups. Rate differences between groups were compared with Fisher exact tests adjusted for multiple comparisons using a resampling bootstrap approach (SAS MULTTEST) for sets of related variables (e.g., symptoms, diseases and conditions, and reproductive outcomes). To examine the effect of multiple exposures in the exposed (study) group by itself, logistic regression analysis of the number of studies in which subjects were enrolled was used. To examine the possibility that confounder variables could explain group differences, further analysis was done using logistic regression analysis of demographic variables. Subgroup analysis was conducted based on class of exposure (vaccine, pathogen, or therapeutic agent). Effects of individual agents were assessed; however, sample sizes were insufficient for conclusive results. All analyses used SAS version 8.2 (SAS Institute, Cary, North Carolina).

The statistical power of this study to detect rate differences between groups was assessed using a power analysis program.[7] With the sample sizes of 358 control subjects and 164 study subjects, with testing at the 5% level of significance (one-tailed), a minimal difference in relative risk (RR) of twofold could be detected with at least 80% probability for rates of health-related outcomes, over a range of background health condition rates for the control subjects.

Results

Study Population Characteristics

Study subjects were male and predominantly (91.0%) Caucasian. The median duration of assignment at Fort Detrick was 2.0 years (range, 0–8 years). The mean age of the population at the time that the survey was performed was 58.4 years (range, 46–79 years); the majority of study subjects were highly educated (58.2% possessed college or graduate degrees). Although 12.8% of those completing surveys were retired at the time of the study, less than one-half (47.9%) were fully employed. No demographic differences were found between subjects who had been exposed to test agents in the course of participation in clinical research studies and those who had served as control subjects for the same studies (Table I).

Eighty-seven percent of the study participants reported their current state of health as good or excellent, and 72.6% claimed to engage in at least some exercise every week. Exposed and control subjects did not differ with regard to current overall health status or current exercise level (Table II).

A relatively small proportion of individuals reported tobacco and/or alcohol use. Only 14.9% of survey respondents admitted to having ever smoked cigarettes, 7.7% to having ever smoked cigars, 7.9% to having ever smoked a pipe, and 1.1% to having ever used chewing tobacco or snuff. Aside from a slightly higher percentage of subjects who had been exposed to test agents claiming to have quit smoking cigarettes, no differences between the exposed and control groups with regard to tobacco and alcohol consumption were evident (Table II).

Exposures

Among the 358 exposed subjects, 303 participated in one study while assigned to Fort Detrick, 75 participated in two studies, 17 participated in three studies, and 1 participated in four studies. Vaccine exposures included Venezuelan equine encephalitis (73 persons), tularemia (45 persons), yellow fever

TABLE I

DEMOGRAPHIC DATA

	Study (n = 358)	Control (n = 164)	p^a
Race (%)			
Caucasian	90.8	91.5	0.832
African American	3.6	4.3	
Other	5.3	4.3	
Male	100.0	100.0	NT
Mean age, years (range)	58.4 (47–74)	58.5 (46–79)	0.822
Mean time spent at Fort Detrick, years (range)	1.5 (<1–8)	1.5 (<1–3)	0.635
Served in military (%)	100.0	100.0	NT
College degree or higher (%)	55.9	63.4	0.126
Current employment status (%)			
Retired	11.7	15.2	0.145
Employed full-time	51.1	40.9	
Employed part-time	31.0	38.4	
Not working because of disability	5.6	5.5	

[a] Tests are two-tailed. NT, not tested.

TABLE II

HEALTH AND BEHAVIORAL CHARACTERISTICS

	Study (n = 358)	Control (n = 164)	p^a
Current health status (%)			0.375
Excellent	39.4	47.6	
Good	46.6	41.5	
Fair	10.6	9.1	
Poor	2.8	1.8	
Current exercise level (%)			0.579
None	25.4	20.1	
More than 5 times/week	10.9	10.4	
Up to 5 times/week	60.1	65.9	
Disabled	3.1	3.0	
Tobacco history			
Ever smoked cigarettes (%)	14.8	15.2	0.896
No. of packs/day (mean)	1.0	1.5	0.285
No. of years smoked (mean)	10.0	11.8	0.500
Quit (among those ever smoked) (%)	96.2	80.0	0.031
Years since quitting (mean)	23.0	16.5	0.084
Ever smoked pipe (%)	7.5	8.5	0.726
Ever smoked cigars (%)	7.8	7.3	1.000
Ever dipped snuff/used chewing tobacco (%)	1.4	0.6	0.670
Alcohol use, ever drink (%)	15.1	19.5	0.206

[a] Tests are two-tailed.

(31 persons), Eastern equine encephalitis (29 persons), Western equine encephalitis (28 persons), plague (13 persons), Q fever (11 persons), Rift Valley fever (8 persons), anthrax (7 persons), chikungunya (six persons), and adenovirus (4 persons). Virulent agent exposures included *Coxiella burnetii* (Q fever) (58 persons), sand fly fever (30 persons), staphylococcal enterotoxin B (20 persons), *Francisella tularensis* (tularemia) (11 persons), Venezuelan equine encephalitis (7 persons), and *Pseudomonas* endotoxin (2 persons). Antibiotic and other therapeutic agent exposures included tetracycline (25 persons), amino acids (15 persons), chloramphenicol (4 persons), and tyrosine (4 persons). Subjects who volunteered to participate in virulent bacterial agent exposure studies (e.g., Q fever or tularemia) also received curative antibiotics during, or at the conclusion of, each project.

Outcomes

Most (87%) study participants reported having had children. The proportions of exposed and control subjects with children were similar (87.4% and 86.0%, respectively). A total of 1,052 children were reported to have been sired by the 522 study participants. The vast majority (92.3%) of these children were reported as normal and healthy. No differences between exposed and control groups in the numbers of children per individual, children with congenital abnormalities, or children with mental retardation were seen (Table III).

No differences between exposed subjects and control subjects were seen with regard to self-reported clinical signs and symptoms or diseases (or other medical conditions) (Tables IV and V). When symptoms and diseases among individuals who had received all vaccines and those who had received all virulent agents were examined separately, there remained no differences between the groups. Asthma was reported more frequently among the group of subjects exposed to all antibiotics or other nonagents than among control subjects (13.0% vs. 2.4%, RR = 6.00, 95% confidence interval [CI] = 1.03–34.9, $p = 0.050$, after adjustment for multiple comparisons).

Attempts to assess frequencies of clinical signs and symptoms or diseases by individual vaccine, individual virulent agent, and individual antibiotic/other agent exposure yielded numbers too small for meaningful analysis for all except recipients of Venezuelan equine encephalitis vaccine(s), tularemia vaccine(s), or virulent *C. burnetii*. Among these exposures, a possible association between asthma and receipt of tularemia vaccine(s) was observed (13.3% of vaccinees vs. 2.4% of control subjects, RR = 6.15, 95% CI = 1.03–36.70, $p = 0.049$, after adjustment for multiple comparisons). In the same cohort, an association with an increased frequency of headaches (never or rarely a problem vs. occasionally or more frequently a problem) among tularemia vaccinees was suggested (35.6% vs. 18.3%), but the difference from control subjects did not reach statistical significance (RR = 2.46, 95% CI = 0.99–6.15, $p = 0.074$, after adjustment for multiple comparisons). There were no differences in any outcome variables (general health, exercise levels, reproductive outcomes, reported symptoms, or reported medical conditions) between subjects participating in one study and those participating in two or more studies (data not shown).

TABLE III

REPRODUCTIVE OUTCOMES

	Study (n = 358)	Control (n = 164)	p^a
No. of children, mean (range)	2.0 (0–7)	2.0 (0–6)	0.502
Had any children	313 (87.4%)	141 (86.0%)	0.647
Had children with birth defects or mental retardation	25 (7.0%)	15 (9.1%)	0.381
No. of children (N = 1,052)			
"Normal/healthy"	698 (95.6%)	306 (95.0%)	0.540
With birth/congenital defects	24 (3.3%)	14 (4.3%)	
With mental retardation	8 (1.1%)	2 (0.6%)	

[a] Tests are two-tailed.

TABLE IV

SELF-REPORTED DISEASES AND CONDITIONS

Condition	Study No.	Study %	Control No.	Control %	p^a
Amyloidosis	0	0.0	0	0.0	1.000
Anemia	6	1.7	2	1.2	1.000
Anemia of chronic disease	1	0.3	0	0.0	1.000
Aplastic anemia	0	0.0	0	0.0	1.000
Arthritis	55	15.4	25	15.2	1.000
Asthma	25	7.0	4	2.4	0.165
Atopic dermatitis	2	0.6	2	1.2	1.000
Cancer	26	7.3	17	10.4	1.000
Diabetes mellitus	25	7.0	17	10.4	1.000
Eczema	13	3.6	5	3.0	1.000
Erythema nodosum	1	0.3	0	0.0	1.000
Frequent colds	20	5.6	8	4.9	0.998
Glomerulonephritis	0	0.0	2	1.2	1.000
Goodpasture's syndrome	0	0.0	0	0.0	1.000
Guillain-Barré syndrome	2	1.2	1	0.3	1.000
Hay fever	55	15.4	26	15.9	1.000
Hemolytic anemia	0	0.0	2	1.2	1.000
Hodgkin's disease	0	0.0	0	0.0	1.000
Hypertension	78	21.8	41	25.0	1.000
Immune complex disease	1	0.3	1	0.6	1.000
Iron deficiency anemia	1	0.3	2	1.2	1.000
Kidney disease	8	2.2	12	7.3	1.000
Leukemia	0	0.0	1	0.6	1.000
Low white blood cell count	9	2.5	2	1.2	0.964
Lupus	0	0.0	0	0.0	1.000
Multiple myeloma	0	0.0	0	0.0	1.000
Multiple sclerosis	1	0.3	0	0.0	1.000
Neuritis	2	0.6	0	0.0	1.000
Parkinson's disease	3	0.8	1	0.6	1.000
Platelet problems	3	0.8	3	1.8	1.000
Pneumonia	43	12.0	24	14.6	1.000
Pneumonitis	1	0.3	0	0.0	1.000
Reiter's syndrome	1	0.3	1	0.6	1.000
Rheumatoid arthritis	4	1.1	3	1.8	1.000
Sarcoidosis	2	0.6	2	1.2	1.000
Serum sickness	0	0.0	0	0.0	1.000
Sjögren's syndrome	0	0.0	0	0.0	1.000
Temporal arteritis	1	0.3	1	0.6	1.000
Thyroid disease	11	3.1	7	4.3	1.000
Ulcers	23	6.4	7	4.3	0.938
Uveitis	2	0.6	0	0.0	1.000
Vasculitis	0	0.0	2	1.2	1.000
Vitamin B_{12} deficiency	2	0.6	1	0.6	1.000
Wegener's granulomatosis	0	0.0	0	0.0	1.000
Total	427		222		

[a] One-tailed Fisher exact test adjusted for multiple comparisons (bootstrap).

TABLE V

SELF-REPORTED SYMPTOMS

Symptom	Study, No.	Control, No.	Study, %	Control, %	p^a
Arthralgia					
Severe	31	15	8.7	9.1	0.488
Moderate	126	49	35.2	29.9	
Mild/none	201	100	56.1	61.0	
Fatigue					
Severe	26	7	7.3	4.3	0.204
Moderate	100	39	27.9	23.8	
Mild/none	232	118	64.8	72.0	
Myalgia					
Severe	10	7	2.8	4.3	0.671
Moderate	80	37	22.3	22.6	
Mild/none	268	120	74.9	73.2	
Insomnia					
Severe	24	12	6.7	7.3	0.799
Moderate	97	40	27.1	24.4	
Mild/none	237	112	66.2	68.3	
Depression					
Severe	13	8	3.6	4.9	0.419
Moderate	53	18	14.8	11.0	
Mild/none	292	138	81.6	84.1	
Memory loss					
Severe	9	5	2.5	3.0	0.939
Moderate	51	23	14.2	14.0	
Mild/none	298	136	83.2	82.9	
Abdominal pain					
Severe	4	2	1.1	1.2	0.357
Moderate	46	14	12.8	8.5	
Mild/none	308	148	86.0	90.2	
Headache					
Severe	6	1	1.7	0.6	0.504
Moderate	71	29	19.8	17.7	
Mild/none	281	134	78.5	81.7	
Malaise					
Severe	18	6	5.0	3.7	0.593
Moderate	47	18	13.1	11.0	
Mild/none	293	140	81.8	85.4	
Tremors					
Severe	1	1	0.3	0.6	0.676
Moderate	13	8	3.6	4.9	
Mild/none	344	155	96.1	94.5	
Fevers					
Severe	0	0	0.0	0.0	0.653[b]
Moderate	17	6	4.7	3.7	
Mild/none	341	158	95.3	96.3	
Rashes					
Severe	4	2	1.1	1.2	0.746
Moderate	31	11	8.7	6.7	
Mild/none	323	151	90.2	92.1	

[a] Comparisons by χ^2 test except as noted.
[b] Two-tailed Fisher exact test.

Discussion

Men entering military service between 1955 and 1973 who volunteered to serve at Fort Detrick in Project Whitecoat participated in a wide variety of clinical research studies involving exposure to investigational vaccines, pathogenic agents, other biologicals (such as antibiotics), and environmental stresses, for the purpose of preparing our nation against the threat of biological warfare. Most, but not all, Project Whitecoat participants were members of the Seventh Day Adventist Church. Individuals were recruited from the ranks of enlisted soldiers (predominantly draftees) with a 1-A-O (conscientious objector) classification who were engaged in basic or advanced individual training at the Medical Training Center, Fort Sam Houston, Texas. Upon arrival at Fort Detrick, personnel underwent a complete series of medical evaluations (including detailed history, physical examination, and laboratory studies) and then were assigned to a variety of duties within the Medical Research

Unit/USAMRIID, such as laboratory technician, animal caretaker, medic, or supply clerk. All duties were noncombatant in nature. All remained full-time soldiers, and most remained at Fort Detrick for the duration of their service obligations. No special consideration or privileges were accorded Project Whitecoat participants.

When volunteers were needed for specific research studies, a briefing to an assembly of Project Whitecoat personnel was provided by the commanding officer, regarding the nature and purpose of the project, the risks involved, and the requirements for each participant. Questions were then entertained. Those expressing interest in participating were subsequently interviewed individually; details of the study were recounted, individuals were allowed to ask questions, and, if the individual again expressed interest in participating, signed consent was obtained (USAMRIID 1969 Fact Sheet, cited in Ref. 8).

During the course of the program, Project Whitecoat volunteers participated in approximately 150 studies.[8] Although some of the projects remain classified, the vast majority of the work was conducted openly and was reported in the scientific and medical literature. No fatalities directly attributable to participation in these clinical trials occurred. Although the trials met and often exceeded the ethical standards of the day for research involving human subjects, the current clinical research climate would preclude repetition of many of these studies today. The data obtained from research involving Project Whitecoat volunteers therefore stand as unique and represent the only human data available in many areas.

To date, there has been no systematic attempt to assess the long-term impact of these exposures on the health of Project Whitecoat volunteers. In 1991–1992, a questionnaire designed to capture reflections on their experiences, the reasons behind their interest in participating in the program, and demographic profiles was completed by approximately 200 former participants.[4] One question in this survey addressed potential residual effects of program participation on health. At that time, only one individual in the program had been awarded a service-connected disability designation. A "few" other Project Whitecoat participants cited program participation as a cause of current medical problems; none was confirmed by medical review.[4,8] The current study was an attempt to objectively assess the impact of participation in clinical research studies by the Project Whitecoat population by comparing questionnaire responses from those who were exposed to agents, biologicals, or other potential stressors and those in the program who served as control subjects for the experiments.

Analyses of questionnaires completed by volunteers for this study provided no evidence that exposures sustained by participants in Project Whitecoat were associated with adverse health outcomes. The exposed and control groups were comparable in most demographic and lifestyle parameters. No differences were reported in overall health status between the two groups, and there were no evident effects on reproductive outcomes. Asthma was reported more frequently among subjects exposed to antibiotics or other inert substances than among control subjects, and similar borderline higher frequencies were observed for reported asthma and headaches among subjects exposed to tularemia vaccines. However, the size of the population under study proved insufficient to conclude that these statistical associations were real.

This study has a number of shortcomings. Mortality rates could not be assessed because of incomplete reporting for the total Project Whitecoat population. There are selection and other biases inherent in a volunteer study of this nature, which might have affected our findings. The sample sizes available were insufficient to detect rare health effects. Furthermore, no laboratory studies were performed as part of the study, and no review of medical records was attempted. Therefore, health consequences from exposures experienced by Project Whitecoat participants might have been missed. However, the dearth of evidence suggesting adverse health effects reported by the volunteers who agreed to participate argues against such a possibility.

Project Whitecoat represents an important chapter in the history of medical defense against biological weapons and in human experimentation. The men who volunteered to participate in the seminal studies that provided proof of concept in so many critical areas should be heralded for their contributions to science and medicine in both the military and civilian sectors. It is gratifying that no adverse impact on the overall health of Project Whitecoat volunteers could be conclusively attributed to their participation in these important research studies.

References

1. Clendenin RM: Science and Technology at Fort Detrick 1943–1968. Washington, DC, U.S. Army, 1968.
2. Smart JK: History of chemical and biological warfare: an American perspective. In: Medical Aspects of Chemical and Biological Warfare, pp 9–85. Edited by Sidell FR, Takafuji ET, Franz DR. Washington, DC, Borden Institute, Walter Reed Army Medical Center, 1997.
3. Cole LA: Clouds of Secrecy: The Army's Germ Warfare Tests over Populated Areas. Totowa, NJ, Rowman and Littlefield, 1988.
4. Mole RL, Mole DM: For God and Country: Operation Whitecoat: 1954–1973. Brushton, NY, Reach Services, 1998.
5. Department of Homeland Security: 2004 Department of Homeland Security Appropriations Act (HR 2555), October 1, 2003.
6. Anderson AO: A brief history of military contributions to ethical standards for research involving human subjects. 2003. Available at http://www.geocities.com/artnscience/jm4-primr.html.
7. Borenstein M, Rothstein H, Cohen J: Power and Precision. Englewood, NJ, Biostat, 2001.
8. Moreno JD: Undue Risk: Secret State Experiments on Humans. New York, NY, W.H. Freeman and Co., 2000.